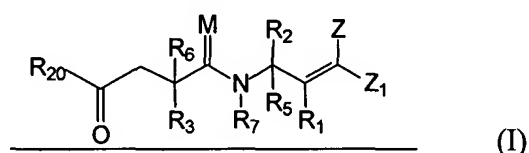


IN THE CLAIMS:

1-29. (Canceled).

30. (Currently Amended) A method of treating a mammalian disease condition mediated by picornaviral protease activity that comprises the step of administering to a mammal in need thereof a therapeutically effective amount of at least one compound ~~as defined in claim 1 or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof~~ of the formula (I):

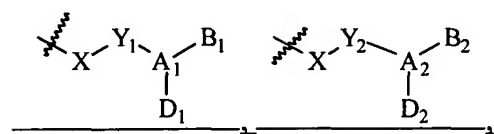


wherein

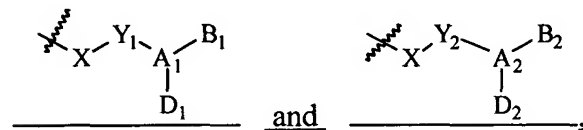
M is O or S;

R<sub>1</sub> is H, F, an alkyl group, OH, SH, or an O-alkyl group;

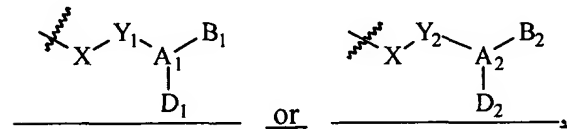
R<sub>2</sub> and R<sub>5</sub> are independently selected from H,



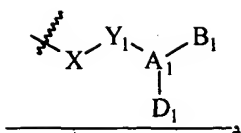
or an alkyl group, wherein said alkyl group is different from



with the proviso that at least one of R<sub>2</sub> or R<sub>5</sub> must be



and wherein, when R<sub>2</sub> or R<sub>5</sub> is



X is =CH or =CF and Y<sub>1</sub> is =CH or =CF,

or X and Y<sub>1</sub> together with Q' form a three-membered ring in which Q' is -C(R<sub>10</sub>)(R<sub>11</sub>)- or -O-, X is -CH- or -CF-, and Y<sub>1</sub> is -CH-, -CF-, or -C(alkyl)-, where R<sub>10</sub> and R<sub>11</sub> independently are H, a halogen, or an alkyl group, or, together with the carbon atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group,

or X is -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, or -S-, and Y<sub>1</sub> is -O-, -S-, -NR<sub>12</sub>-, -C(R<sub>13</sub>)(R<sub>14</sub>)-, -C(O)-, -C(S)-, or -C(CR<sub>13</sub>R<sub>14</sub>)-,

wherein R<sub>12</sub> is H or alkyl, and R<sub>13</sub> and R<sub>14</sub> independently are H, F, or an alkyl group, or, together with the atoms to which they are bonded, form a cycloalkyl group or a heterocycloalkyl group;

A<sub>1</sub> is C, CH, CF, S, P, Se, N, NR<sub>15</sub>, S(O), Se(O), P-OR<sub>15</sub>, or P-NR<sub>15</sub>R<sub>16</sub>,

wherein R<sub>15</sub> and R<sub>16</sub> independently are an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom to which they are bonded, form a heterocycloalkyl group;

D<sub>1</sub> is a moiety with a lone pair of electrons capable of forming a hydrogen bond;

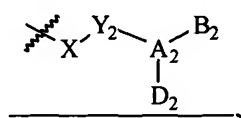
and

B<sub>1</sub> is H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -OR<sub>17</sub>-, -SR<sub>17</sub>-, -NR<sub>17</sub>R<sub>18</sub>-, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>- or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

and with the provisos that when D<sub>1</sub> is the moiety ≡N with a lone pair of electrons capable of forming a hydrogen bond, B<sub>1</sub> does not exist; and when A<sub>1</sub> is an sp<sup>3</sup> carbon, B<sub>1</sub> is not -

NR<sub>17</sub>R<sub>18</sub> when D<sub>1</sub> is the moiety -NR<sub>25</sub>R<sub>26</sub> with a lone pair of electrons capable of forming a hydrogen bond, wherein R<sub>25</sub> and R<sub>26</sub> are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group;  
and wherein D<sub>1</sub>-A<sub>1</sub>-B<sub>1</sub> optionally forms a nitro group where A<sub>1</sub> is N;  
and further wherein, when R<sub>2</sub> or R<sub>5</sub> is



X is =CH or =CF and Y<sub>2</sub> is =C, =CH, or =CF,

or X and Y<sub>2</sub> together with Q' form a three-membered ring in which Q' is -C(R<sub>10</sub>)(R<sub>11</sub>)- or -O-, X is -CH- or -CF-, and Y<sub>2</sub> is -CH-, -CF-, or -C(alkyl)-, where R<sub>10</sub> and R<sub>11</sub> independently are H, a halogen, or an alkyl group, or, together with the carbon atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group,

or X is -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, or -S-, and Y<sub>2</sub> is -O-, -S-, -N(R'<sub>12</sub>)-, -C(O)-, -C(R'<sub>13</sub>)(R'<sub>14</sub>)-, -C(S)-, or -C(CR'<sub>13</sub>R'<sub>14</sub>)-, wherein R'<sub>12</sub> is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -OR'<sub>13a</sub>-, NR'<sub>13</sub>R'<sub>14a</sub>-, -C(O)-R'<sub>13a</sub>-, -SO<sub>2</sub>R'<sub>13a</sub> or -C(S)R'<sub>13a</sub>, and R'<sub>13</sub> and R'<sub>14</sub> independently are H, F, or an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group;

A<sub>2</sub> is C, CH, CF, S, P, Se, N, NR<sub>15</sub>, S(O), Se(O), P-OR<sub>15</sub>, or P-NR<sub>15</sub>R<sub>16</sub>,

wherein R<sub>15</sub> and R<sub>16</sub> independently are an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom to which they are bonded, form a heterocycloalkyl group;

D<sub>2</sub> is a moiety with a lone pair of electrons capable of forming a hydrogen bond;  
and

B<sub>2</sub> is H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl  
group, a heteroaryl group, -OR<sub>17</sub>, -SR<sub>17</sub>, -NR<sub>17</sub>R<sub>18</sub>, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub> or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub> and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl  
group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an  
acyl group;

and further wherein any combination of Y<sub>2</sub>, A<sub>2</sub>, B<sub>2</sub>, and D<sub>2</sub> optionally can form a  
cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group;

R<sub>3</sub> and R<sub>6</sub> are independently H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl  
group, an aryl group, a heteroaryl group, -C(O)R<sub>17</sub>, -OR<sub>17</sub>, -SR<sub>17</sub>, -NR<sub>17</sub>R<sub>18</sub>, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>,  
or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a  
heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

or, R<sub>3</sub> and R<sub>6</sub>, together with the carbon atom to which they are attached, form a cycloalkyl  
group or a heterocycloalkyl group;

R<sub>7</sub> is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a  
heteroaryl group, -OR<sub>17</sub>, -SR<sub>17</sub>, -NR<sub>17</sub>R<sub>18</sub>, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>, or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a  
heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

or R<sub>7</sub>, together with R<sub>3</sub> or R<sub>6</sub> and the atoms to which they are attached, forms a  
heterocycloalkyl group;

R<sub>20</sub> is H, OH, or any suitable organic moiety; and

Z and Z<sub>1</sub> are independently H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl  
group, an aryl group, a heteroaryl group, -C(O)R<sub>21</sub>, -CO<sub>2</sub>R<sub>21</sub>, -CN, -C(O)NR<sub>21</sub>R<sub>22</sub>, -  
C(O)NR<sub>21</sub>OR<sub>22</sub>, -C(S)R<sub>21</sub>, -C(S)NR<sub>21</sub>R<sub>22</sub>, -NO<sub>2</sub>, -SOR<sub>21</sub>, -SO<sub>2</sub>R<sub>21</sub>, -SO<sub>2</sub>NR<sub>21</sub>R<sub>22</sub>, -  
SO(NR<sub>21</sub>)(OR<sub>22</sub>), -SONR<sub>21</sub>, -SO<sub>3</sub>R<sub>21</sub>, -PO(OR<sub>21</sub>)<sub>2</sub>, -PO(R<sub>21</sub>)(R<sub>22</sub>), -PO(NR<sub>21</sub>R<sub>22</sub>)(OR<sub>23</sub>),

PO(NR<sub>21</sub>R<sub>22</sub>)(NR<sub>23</sub>R<sub>24</sub>), -C(O)NR<sub>21</sub>NR<sub>22</sub>R<sub>23</sub>, or -C(S)NR<sub>21</sub>NR<sub>22</sub>R<sub>23</sub>,

wherein R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, and R<sub>24</sub> are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, an acyl group, or a thioacyl group, or wherein any two of R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, and R<sub>24</sub>, together with the atom(s) to which they are bonded, form a heterocycloalkyl group;

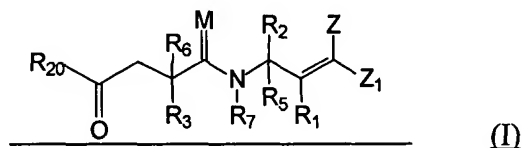
or Z<sub>1</sub>, as defined above, together with R<sub>1</sub>, as defined above, and the atoms to which Z<sub>1</sub> and R<sub>1</sub> are bonded, form a cycloalkyl or heterocycloalkyl group,

or Z and Z<sub>1</sub>, both as defined above, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group;

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof;

and wherein said compound, or pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof, has antipicornaviral activity with an EC<sub>50</sub> less than or equal to 10 μM in the HI-HeLa cell culture assay.

31. (Currently amended) A method of inhibiting the activity of a picornaviral 3C protease that comprises the step of contacting the picornaviral 3C protease with an effective amount of at least one compound ~~as defined in claim 1~~ or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof of the formula (I):

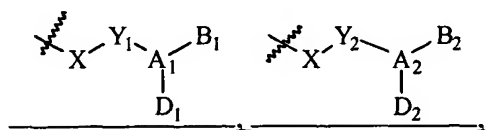


wherein

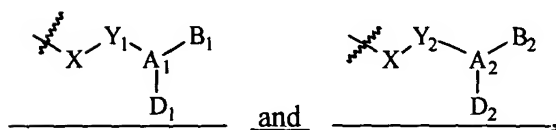
M is O or S;

R<sub>1</sub> is H, F, an alkyl group, OH, SH, or an O-alkyl group;

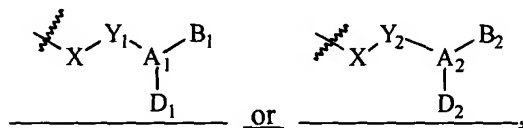
R<sub>2</sub> and R<sub>5</sub> are independently selected from H,



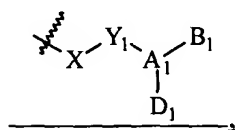
or an alkyl group, wherein said alkyl group is different from



with the proviso that at least one of R<sub>2</sub> or R<sub>5</sub> must be



and wherein, when R<sub>2</sub> or R<sub>5</sub> is



X is =CH or =CF and Y<sub>1</sub> is =CH or =CF,

or X and Y<sub>1</sub> together with Q' form a three-membered ring in which Q' is -

C(R<sub>10</sub>)(R<sub>11</sub>)- or -O-, X is -CH- or -CF-, and Y<sub>1</sub> is -CH-, -CF-, or -C(alkyl)-,

where R<sub>10</sub> and R<sub>11</sub> independently are H, a halogen, or an alkyl group, or,

together with the carbon atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group.

or X is -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, or -S-, and Y<sub>1</sub> is -O-, -S-, -NR<sub>12</sub>-, -C(R<sub>13</sub>)(R<sub>14</sub>)-, -

C(O)-, -C(S)-, or -C(CR<sub>13</sub>R<sub>14</sub>)-,

wherein R<sub>12</sub> is H or alkyl, and R<sub>13</sub> and R<sub>14</sub> independently are H, F, or

an alkyl group, or, together with the atoms to which they are bonded,

form a cycloalkyl group or a heterocycloalkyl group;

A<sub>1</sub> is C, CH, CF, S, P, Se, N, NR<sub>15</sub>, S(O), Se(O), P-OR<sub>15</sub>, or P-NR<sub>15</sub>R<sub>16a</sub>

wherein R<sub>15</sub> and R<sub>16</sub> independently are an alkyl group, a cycloalkyl group, a

heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together

with the atom to which they are bonded, form a heterocycloalkyl group;

D<sub>1</sub> is a moiety with a lone pair of electrons capable of forming a hydrogen bond;

and

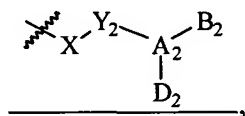
B<sub>1</sub> is H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -OR<sub>17</sub>, -SR<sub>17</sub>, -NR<sub>17</sub>R<sub>18</sub>, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub> or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

and with the provisos that when D<sub>1</sub> is the moiety ≡N with a lone pair of electrons capable of forming a hydrogen bond, B<sub>1</sub> does not exist; and when A<sub>1</sub> is an sp<sup>3</sup> carbon, B<sub>1</sub> is not -NR<sub>17</sub>R<sub>18</sub> when D<sub>1</sub> is the moiety -NR<sub>25</sub>R<sub>26</sub> with a lone pair of electrons capable of forming a hydrogen bond, wherein R<sub>25</sub> and R<sub>26</sub> are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group;

and wherein D<sub>1</sub>-A<sub>1</sub>-B<sub>1</sub> optionally forms a nitro group where A<sub>1</sub> is N;

and further wherein, when R<sub>2</sub> or R<sub>5</sub> is



X is =CH or =CF and Y<sub>2</sub> is =C, =CH, or =CF,

or X and Y<sub>2</sub> together with Q' form a three-membered ring in which Q' is -C(R<sub>10</sub>)(R<sub>11</sub>)- or -O-, X is -CH- or -CF-, and Y<sub>2</sub> is -CH-, -CF-, or -C(alkyl)-, where R<sub>10</sub> and R<sub>11</sub> independently are H, a halogen, or an alkyl group, or, together with the carbon atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group,

or X is -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, or -S-, and Y<sub>2</sub> is -O-, -S-, -N(R'<sub>12</sub>)-, -C(O)-, -C(R'<sub>13</sub>)(R'<sub>14</sub>)-, -C(S)-, or -C(CR'<sub>13</sub>R'<sub>14</sub>)-,

wherein R'<sub>12</sub> is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -OR'<sub>13</sub>, -NR'<sub>13</sub>R'<sub>14</sub>, -C(O)-R'<sub>13</sub>, -SO<sub>2</sub>R'<sub>13</sub>, or -C(S)R'<sub>13</sub>, and R'<sub>13</sub> and R'<sub>14</sub>,

independently are H, F, or an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group;

A<sub>2</sub> is C, CH, CF, S, P, Se, N, NR<sub>15</sub>, S(O), Se(O), P-OR<sub>15</sub>, or P-NR<sub>15</sub>R<sub>16</sub>,

wherein R<sub>15</sub> and R<sub>16</sub> independently are an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom to which they are bonded, form a heterocycloalkyl group;

D<sub>2</sub> is a moiety with a lone pair of electrons capable of forming a hydrogen bond;  
and

B<sub>2</sub> is H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -OR<sub>17</sub>, -SR<sub>17</sub>, -NR<sub>17</sub>R<sub>18</sub>, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>, or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

and further wherein any combination of Y<sub>2</sub>, A<sub>2</sub>, B<sub>2</sub>, and D<sub>2</sub> optionally can form a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group;

R<sub>3</sub> and R<sub>6</sub> are independently H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -C(O)R<sub>17</sub>, -OR<sub>17</sub>, -SR<sub>17</sub>, -NR<sub>17</sub>R<sub>18</sub>, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>, or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

or, R<sub>3</sub> and R<sub>6</sub>, together with the carbon atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group;

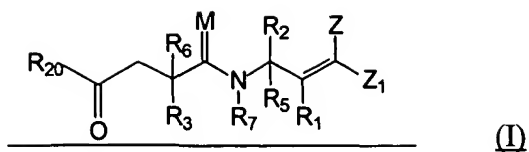
R<sub>7</sub> is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -OR<sub>17</sub>, -SR<sub>17</sub>, -NR<sub>17</sub>R<sub>18</sub>, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>, or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a



heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;  
or R<sub>7</sub>, together with R<sub>3</sub> or R<sub>6</sub> and the atoms to which they are attached, forms a  
heterocycloalkyl group;  
R<sub>20</sub> is H, OH, or any suitable organic moiety; and  
Z and Z<sub>1</sub> are independently H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl  
group, an aryl group, a heteroaryl group, -C(O)R<sub>21</sub>, -CO<sub>2</sub>R<sub>21</sub>, -CN, -C(O)NR<sub>21</sub>, R<sub>22</sub>, -  
C(O)NR<sub>21</sub>, OR<sub>22</sub>, -C(S)R<sub>21</sub>, -C(S)NR<sub>21</sub>, R<sub>22</sub>, -NO<sub>2</sub>, -SOR<sub>21</sub>, -SO<sub>2</sub>R<sub>21</sub>, -SO<sub>2</sub>NR<sub>21</sub>, R<sub>22</sub>, -  
SO(NR<sub>21</sub>)(OR<sub>22</sub>), -SONR<sub>21</sub>, -SO<sub>3</sub>R<sub>21</sub>, -PO(OR<sub>21</sub>)<sub>2</sub>, -PO(R<sub>21</sub>)(R<sub>22</sub>), -PO(NR<sub>21</sub>, R<sub>22</sub>)(OR<sub>23</sub>),  
PO(NR<sub>21</sub>, R<sub>22</sub>)(NR<sub>23</sub>, R<sub>24</sub>), -C(O)NR<sub>21</sub>, NR<sub>22</sub>, R<sub>23</sub>, or -C(S)NR<sub>21</sub>, NR<sub>22</sub>, R<sub>23</sub>,  
wherein R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, and R<sub>24</sub> are independently H, an alkyl group, a cycloalkyl  
group, a heterocycloalkyl group, an aryl group, a heteroaryl group, an acyl group, or  
a thioacyl group, or wherein any two of R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, and R<sub>24</sub>, together with the  
atom(s) to which they are bonded, form a heterocycloalkyl group;  
or Z<sub>1</sub>, as defined above, together with R<sub>1</sub>, as defined above, and the atoms to which Z<sub>1</sub>  
and R<sub>1</sub> are bonded, form a cycloalkyl or heterocycloalkyl group,  
or Z and Z<sub>1</sub>, both as defined above, together with the atoms to which they are bonded,  
form a cycloalkyl or heterocycloalkyl group;  
or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof;  
and wherein said compound, or pharmaceutically acceptable prodrug, salt, active  
metabolite, or solvate thereof, has antipicornaviral activity with an EC<sub>50</sub> less than or equal  
to 10 μM in the HI-HeLa cell culture assay.

32. (Currently Amended) A method of inhibiting the activity of a rhinoviral protease that comprises the step of contacting the rhinoviral protease with an effective amount of at least one compound ~~as defined in claim 1 or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof~~ of the formula (I):

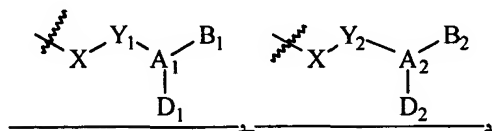


wherein

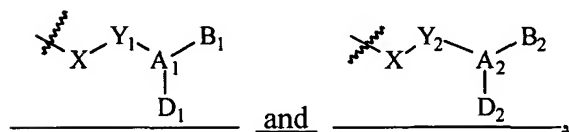
M is O or S;

R<sub>1</sub> is H, F, an alkyl group, OH, SH, or an O-alkyl group;

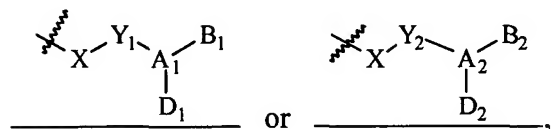
R<sub>2</sub> and R<sub>5</sub> are independently selected from H,



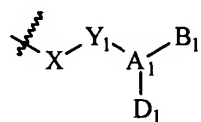
or an alkyl group, wherein said alkyl group is different from



with the proviso that at least one of R<sub>2</sub> or R<sub>5</sub> must be



and wherein, when R<sub>2</sub> or R<sub>5</sub> is



X is =CH or =CF and Y<sub>1</sub> is =CH or =CF,

or X and Y<sub>1</sub> together with Q' form a three-membered ring in which Q' is -

C(R<sub>10</sub>)(R<sub>11</sub>)- or -O-, X is -CH- or -CF-, and Y<sub>1</sub> is -CH-, -CF-, or -C(alkyl)-,

where R<sub>10</sub> and R<sub>11</sub> independently are H, a halogen, or an alkyl group, or,

together with the carbon atom to which they are attached, form a cycloalkyl

group or a heterocycloalkyl group.

or X is -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, or -S-, and Y<sub>1</sub> is -O-, -S-, -NR<sub>12</sub>-, -C(R<sub>13</sub>)(R<sub>14</sub>)-, -C(O)-, -C(S)-, or -C(CR<sub>13</sub>R<sub>14</sub>)-,

wherein R<sub>12</sub> is H or alkyl, and R<sub>13</sub> and R<sub>14</sub> independently are H, F, or an alkyl group, or, together with the atoms to which they are bonded, form a cycloalkyl group or a heterocycloalkyl group;

A<sub>1</sub> is C, CH, CF, S, P, Se, N, NR<sub>15</sub>, S(O), Se(O), P-OR<sub>15</sub>, or P-NR<sub>15</sub>R<sub>16</sub>

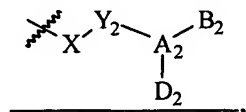
wherein R<sub>15</sub> and R<sub>16</sub> independently are an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together with the atom to which they are bonded, form a heterocycloalkyl group;

D<sub>1</sub> is a moiety with a lone pair of electrons capable of forming a hydrogen bond;  
and

B<sub>1</sub> is H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -OR<sub>17</sub>-, -SR<sub>17</sub>-, -NR<sub>17</sub>R<sub>18</sub>-, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>-, or -NR<sub>17</sub>-OR<sub>18</sub>-,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;

and with the provisos that when D<sub>1</sub> is the moiety ≡N with a lone pair of electrons capable of forming a hydrogen bond, B<sub>1</sub> does not exist; and when A<sub>1</sub> is an sp<sup>3</sup> carbon, B<sub>1</sub> is not -NR<sub>17</sub>R<sub>18</sub> when D<sub>1</sub> is the moiety -NR<sub>25</sub>R<sub>26</sub> with a lone pair of electrons capable of forming a hydrogen bond, wherein R<sub>25</sub> and R<sub>26</sub> are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group;  
and wherein D<sub>1</sub>-A<sub>1</sub>-B<sub>1</sub> optionally forms a nitro group where A<sub>1</sub> is N;  
and further wherein, when R<sub>2</sub> or R<sub>5</sub> is



X is =CH or =CF and Y<sub>2</sub> is =C, =CH, or =CF,

or X and Y<sub>2</sub> together with Q' form a three-membered ring in which Q' is -  
C(R<sub>10</sub>)(R<sub>11</sub>)- or -O-, X is -CH- or -CF-, and Y<sub>2</sub> is -CH-, -CF-, or -C(alkyl)-,  
where R<sub>10</sub> and R<sub>11</sub> independently are H, a halogen, or an alkyl group, or,  
together with the carbon atom to which they are attached, form a cycloalkyl  
group or a heterocycloalkyl group.

or X is -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, or -S-, and Y<sub>2</sub> is -O-, -S-, -N(R'<sub>12</sub>)-, -C(O)-, -  
C(R'<sub>13</sub>)(R'<sub>14</sub>)-, -C(S)-, or -C(CR'<sub>13</sub>R'<sub>14</sub>)-,  
wherein R'<sub>12</sub> is H, an alkyl group, a cycloalkyl group, a  
heterocycloalkyl group, an aryl group, a heteroaryl group, -OR'<sub>13</sub>-,  
NR'<sub>13</sub>R'<sub>14</sub>-, -C(O)-R'<sub>13</sub>-, -SO<sub>2</sub>R'<sub>13</sub>-, or -C(S)R'<sub>13</sub>-, and R'<sub>13</sub> and R'<sub>14</sub>  
independently are H, F, or an alkyl group, a cycloalkyl group, a  
heterocycloalkyl group, an aryl group, or a heteroaryl group, or,  
together with the atom to which they are attached, form a cycloalkyl  
group or a heterocycloalkyl group;

A<sub>2</sub> is C, CH, CF, S, P, Se, N, NR<sub>15</sub>, S(O), Se(O), P-OR<sub>15</sub>, or P-NR<sub>15</sub>R<sub>16</sub>,

wherein R<sub>15</sub> and R<sub>16</sub> independently are an alkyl group, a cycloalkyl group, a  
heterocycloalkyl group, an aryl group, or a heteroaryl group, or, together  
with the atom to which they are bonded, form a heterocycloalkyl group;

D<sub>2</sub> is a moiety with a lone pair of electrons capable of forming a hydrogen bond;

and

B<sub>2</sub> is H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl  
group, a heteroaryl group, -OR<sub>17</sub>-, -SR<sub>17</sub>-, -NR<sub>17</sub>R<sub>18</sub>-, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>-, or -NR<sub>17</sub>OR<sub>18</sub>-,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl  
group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an  
acyl group;

and further wherein any combination of Y<sub>2</sub>, A<sub>2</sub>, B<sub>2</sub>, and D<sub>2</sub> optionally can form a  
cycloalkyl group, a heterocycloalkyl group, an aryl group, or a heteroaryl group;

R<sub>3</sub> and R<sub>6</sub> are independently H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -C(O)R<sub>17</sub>, -OR<sub>17</sub>, -SR<sub>17</sub>, -NR<sub>17</sub>R<sub>18</sub>, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>, or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;  
or, R<sub>3</sub> and R<sub>6</sub>, together with the carbon atom to which they are attached, form a cycloalkyl group or a heterocycloalkyl group;

R<sub>7</sub> is H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -OR<sub>17</sub>, -SR<sub>17</sub>, -NR<sub>17</sub>R<sub>18</sub>, -NR<sub>19</sub>NR<sub>17</sub>R<sub>18</sub>, or -NR<sub>17</sub>OR<sub>18</sub>,

wherein R<sub>17</sub>, R<sub>18</sub>, and R<sub>19</sub> independently are H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, or an acyl group;  
or R<sub>7</sub>, together with R<sub>3</sub> or R<sub>6</sub> and the atoms to which they are attached, forms a heterocycloalkyl group;

R<sub>20</sub> is H, OH, or any suitable organic moiety; and

Z and Z<sub>1</sub> are independently H, F, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, -C(O)R<sub>21</sub>, -CO<sub>2</sub>R<sub>21</sub>, -CN, -C(O)NR<sub>21</sub>R<sub>22</sub>, -C(O)NR<sub>21</sub>OR<sub>22</sub>, -C(S)R<sub>21</sub>, -C(S)NR<sub>21</sub>R<sub>22</sub>, -NO<sub>2</sub>, -SOR<sub>21</sub>, -SO<sub>2</sub>R<sub>21</sub>, -SO<sub>2</sub>NR<sub>21</sub>R<sub>22</sub>, -SO(NR<sub>21</sub>)(OR<sub>22</sub>), -SONR<sub>21</sub>, -SO<sub>3</sub>R<sub>21</sub>, -PO(OR<sub>21</sub>)<sub>2</sub>, -PO(R<sub>21</sub>)(R<sub>22</sub>), -PO(NR<sub>21</sub>R<sub>22</sub>)(OR<sub>23</sub>), -PO(NR<sub>21</sub>R<sub>22</sub>)(NR<sub>23</sub>R<sub>24</sub>), -C(O)NR<sub>21</sub>NR<sub>22</sub>R<sub>23</sub>, or -C(S)NR<sub>21</sub>NR<sub>22</sub>R<sub>23</sub>,

wherein R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, and R<sub>24</sub> are independently H, an alkyl group, a cycloalkyl group, a heterocycloalkyl group, an aryl group, a heteroaryl group, an acyl group, or a thioacyl group, or wherein any two of R<sub>21</sub>, R<sub>22</sub>, R<sub>23</sub>, and R<sub>24</sub>, together with the atom(s) to which they are bonded, form a heterocycloalkyl group;  
or Z<sub>1</sub>, as defined above, together with R<sub>1</sub>, as defined above, and the atoms to which Z<sub>1</sub> and R<sub>1</sub> are bonded, form a cycloalkyl or heterocycloalkyl group,  
or Z and Z<sub>1</sub>, both as defined above, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group;

or a pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof;

and wherein said compound, or pharmaceutically acceptable prodrug, salt, active metabolite, or solvate thereof, has antipicornaviral activity with an EC<sub>50</sub> less than or equal to 10  $\mu$ M in the HI-HeLa cell culture assay.

33-34. (Canceled).